Consumer genetics and third-party interpretation tools

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BH 444/544

January 11, 2021

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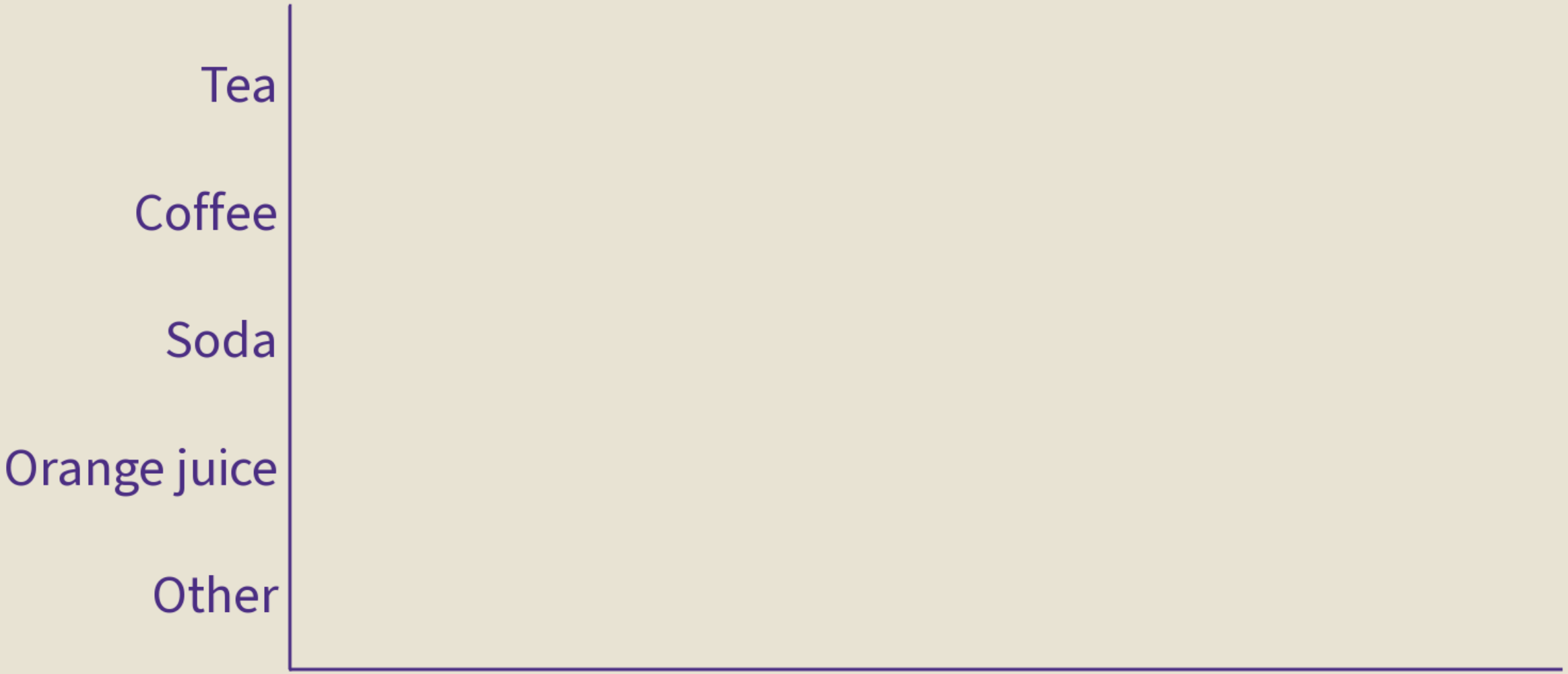
23andMeow?


basepaws
CatKit
THE WORLD'S FIRST AT-HOME
CAT GENETICS TEST
Do NOT
throw away
this box.
It will be used
to return the sample
for processing.

Poll everywhere

- Respond at **PollEv.com/sarahcn** 
- Text **SARAHCN** at **22333** once to join 

Warm-up: what's your preferred morning beverage?



A consumer genetic test can return information about

close family relationships **A**

population history **B**

disease risks **C**

non-medical traits **D**

all of the above **E**

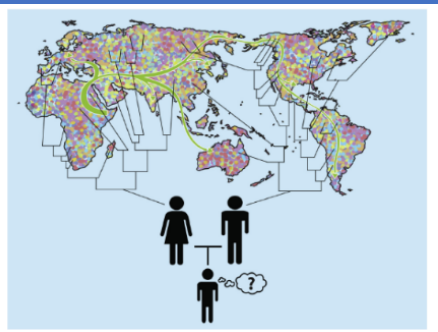
“Many orientedness” of DNA

Family relationships

Ancestry/population history

Disease risk/susceptibility

Non-medical traits



Outline

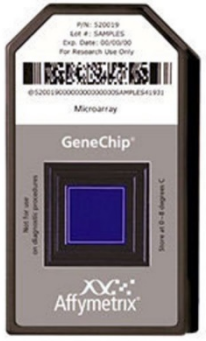
Overview of DTC genetic testing

Potential harms and benefits

Overview of third-party tools

What is direct-to-consumer genetic testing?

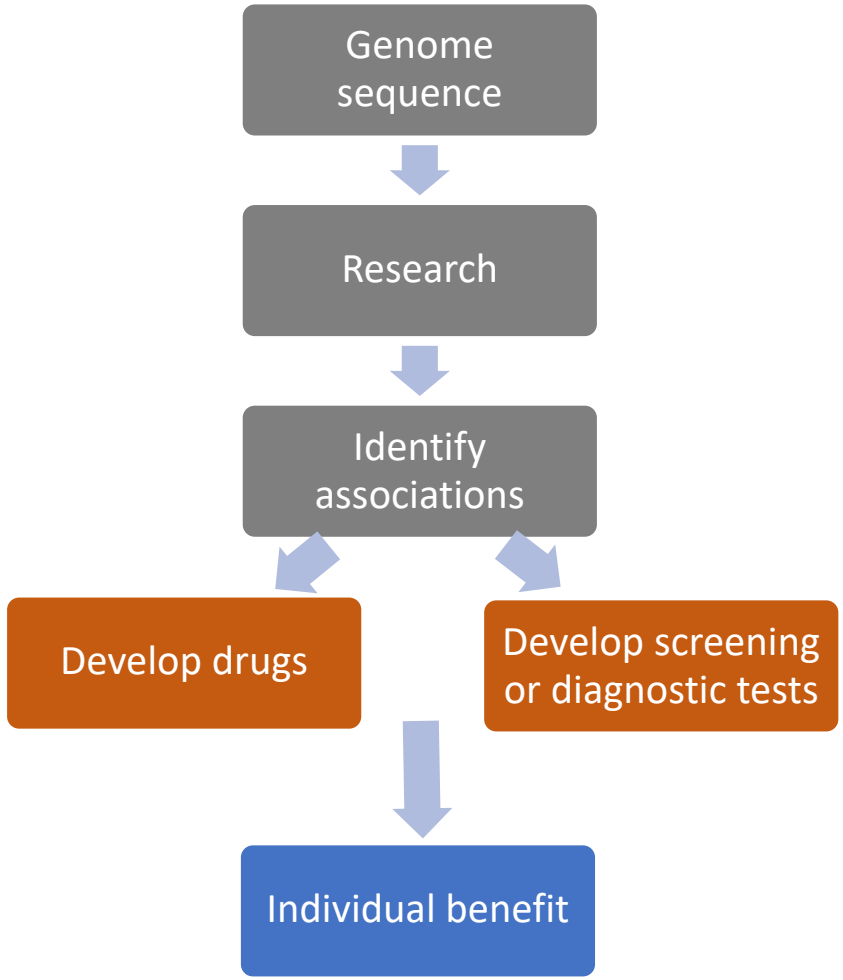
- Genetic testing available without physician intermediary
- Hundreds of companies now offer
- Can report on multiple categories ->
- In part enabled by advancements in genotyping technology (microarrays or “SNP chips” in early 2000’s)



Category	Number of companies	Percentage
Ancestry	74	30%
Athletic	38	15%
Child talent	4	2%
Matchmaking	3	1%
Surreptitious	34	14%
Nutrigenetic	74	30%
Non-legal paternity	88	36%
Legal paternity	83	34%
Genetic relatedness	92	37%
Carrier	27	11%
Only health testing	31	13%
Total companies analyzed	246	

Table adapted from Phillips 2016, https://doi.org/10.1016/j.atg.2016.01.001

Delivering the promise of the HGP



SLOW, EXPENSIVE

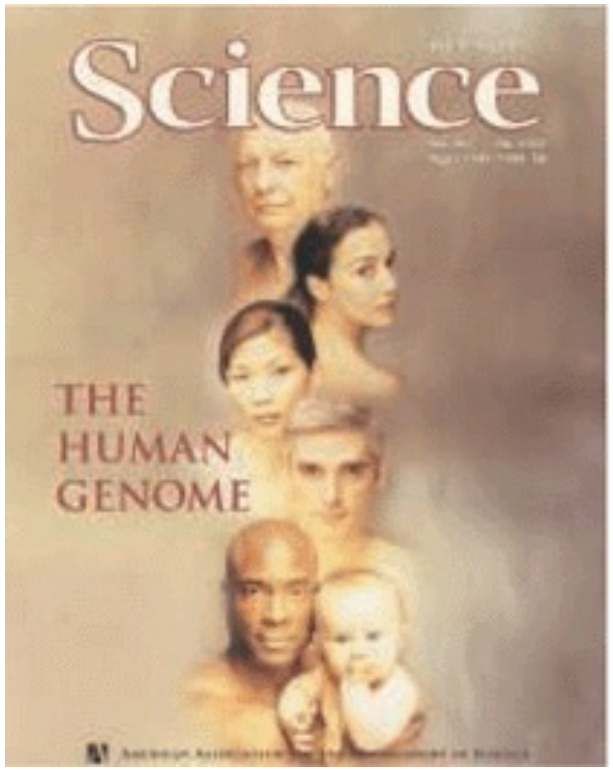
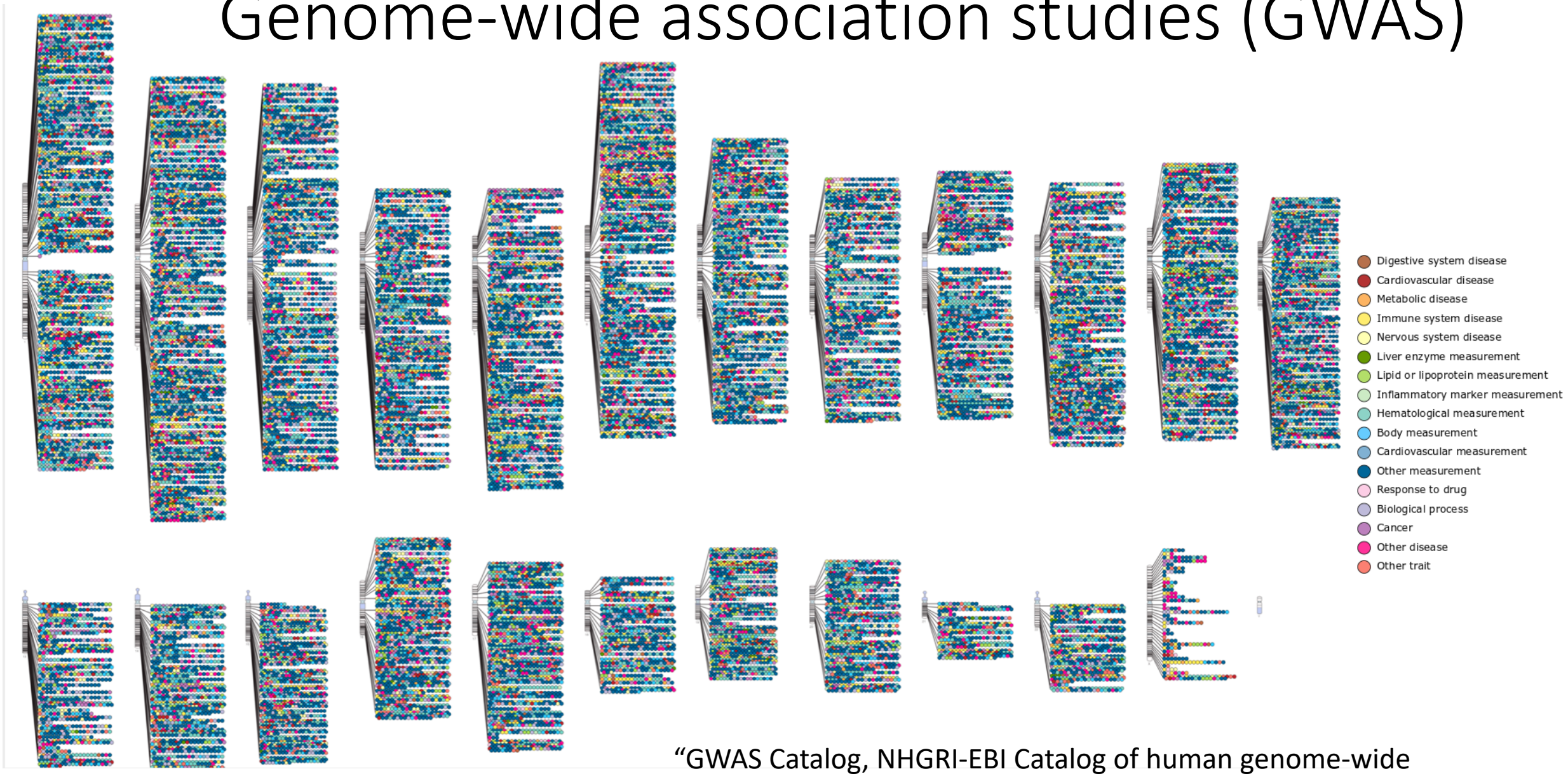


Image from Collins (2011) in *Science*

Genome-wide association studies (GWAS)



"GWAS Catalog, NHGRI-EBI Catalog of human genome-wide association studies," https://www.ebi.ac.uk/gwas

DTC genetic testing process

Customer → **DTC company**

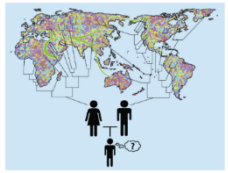
(1) Mail saliva sample using company-provided spit kit

(2) Extracts customer's DNA

(3) Measures (genotypes) DNA at ~1M variants (SNPs)

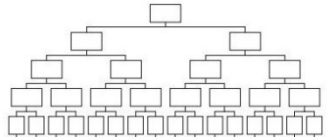
(4) Analyzes **subset** of genotyped variants to provide **interpreted reports**:

Genetic ancestry



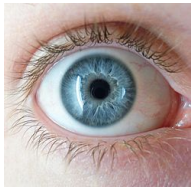
ancestryDNA™ FamilyTreeDNA 23andMe MyHeritage

Genealogy



ancestryDNA™ FamilyTreeDNA 23andMe MyHeritage

Traits



23andMe

Health

23andMe

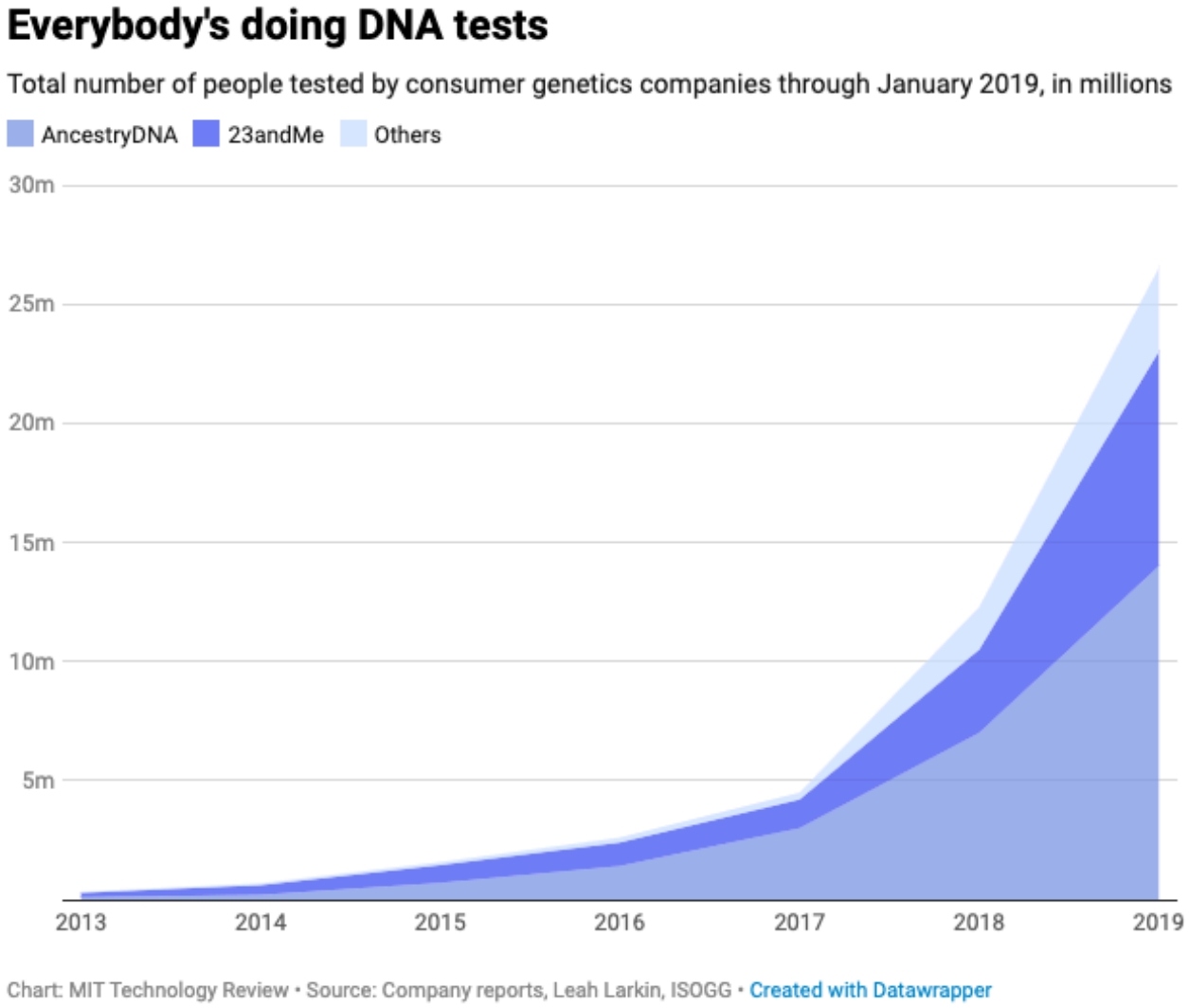
Diet & fitness

DNAFit ATHLETIGEN

(5) Provides to costumer:

- **interpreted reports**
- **raw data** file of all ~1M measured variants

Growing popularity of DTC testing



- 2019 industry estimates
  - 26M total tested
    - 14M Ancestry DNA
    - 9M 23andMe
- Tests purchased in 2018 outnumbered all previous years combined

Regalado, Feb 2019, MIT Technology Review

Concerns about DTC genetic testing

Scientific

- Analytic validity: are DNA variants measured (genotyped) accurately? (*analytic validity*)
- Are interpretations valid?
  - For health results, are the variants linked to disease as claimed by the company? (*clinical validity*)

Regulatory

- Who regulates and how?
  - Food and Drug Administration (FDA)
  - Federal Trade Commission (FTC)
  - Laboratory regulation (CLIA)
- Adequate consumer protection?

DTC companies not completely unregulated

06-05-18

The FTC is investigating DNA firms like 23andMe and Ancestry over privacy

As the DNA testing market has exploded—worth approximately $99 million in 2017 a
expected to increase to $310 million by 2022—concerns have also grown about the u
genetic data.

Charles E.
SCHUMER
UNITED STATES SENATOR FOR NEW YORK

Lea
CON

Newsroom / Press Releases

11.26.17

SCHUMER REVEALS: POPULAR AT HOME DNA TEST KITS ARE PUTTING CONSUMER PRIVACY AT GREAT RISK, AS DNA FIRMS COULD SELL YOUR MOST PERSONAL INFO & GENETIC DATA TO ALL-COMERS; SENATOR PUSHES FEDS TO INVESTIGATE & ENSURE FAIR PRIVACY STANDARDS FOR ALL DNA ?KITS

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

November 02, 2017

23andMe, Inc.
% Ms. Lisa Charter
Director, Regulatory Affairs and Quality Assurance
899 West Evelyn Avenue
Mountain View, CA 94041

Re: DEN160026
23andMe Personal Genome Service (PGS) Test
Evaluation of Automatic Class III Designation – *De Novo* Request
Regulation Number: 21 CFR 866.5950
Regulation Name: Genetic Health Risk Assessment System

Ethical concerns with DTC testing

Individuals

- Psychosocial impacts
- Privacy and data usage
- Effects on families
- Lack of informed consent

Systems

- Drain on health care systems
- Unequal access
- Genetic discrimination

Badalato et al. EJHG 2017; Caulfield and McGuire Annu. Rev. Med. 2012

Potential harms but also potential benefits

Plural utilities	• Lack of medical utility doesn't preclude other personal utilities of genetic info
Enhanced autonomy	• Individuals can choose what information to access about themselves and when
Increasing scientific and genetic literacy	• Customers can engage with research, may pique their interest in science, genetics
"Data play"	• Is "recreational genomics" such a bad thing?

Vayena E. J Med Ethics 2015; Furbo 2016

Autonomy vs benefit

Should individuals be able to pursue DTC testing even when benefits may not be clear or immediate?

Are choices autonomous if caveats are not fully communicated or understood?

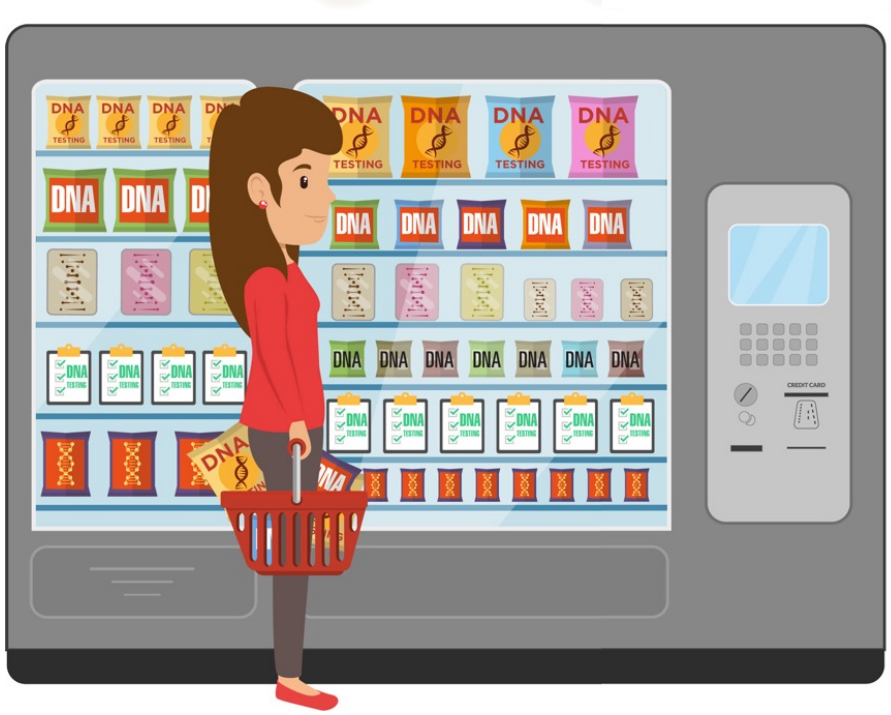


Image: https://www.pharmacytoday.org/article/S1042-0991(20)30212-7

Benefit at aggregate or individual level

- DTC testing takes insights at population or group level and applies them to individuals
- Genetic info clearly valuable in **aggregate**
- Value at **individual** level less clear (for now)
- Feedback loop of discovery
  - DTC companies also perform research on aggregated customer data to make new discoveries and improve products….

DTC company research arms

Since 2010, 23andMe has published 172 papers

23andMe customers who participate in research are helping us advance scientific knowledge in revolutionary new ways. Each discovery helps pave the way for advances in medicine.

JULY 2020

The design of a virtual Parkinson's disease cohort study

Collaboration with University of Rochester — Published in Journal of PD

JUNE 2020

23andMe Maps the Way We Eat

Led by 23andMe — Published in Public Health Nutrition

JUNE 2020

Study suggests that partial LRRK2 inhibition may not have adverse effects

Collaboration with the Broad Institute — Published in Nature

https://www.23andme.com/publications/

AJHG
Volume 96, Issue 1, 8 January 2015, Pages 37-53
CellPress

Article

The Genetic Ancestry of African Americans, Latinos, and European Americans across the United States

Katarzyna Bryc [1, 2], Eric Y. Durand [2], J. Michael Macpherson [3], David Reich [1, 4, 5], Joanna L. Mountain [2]

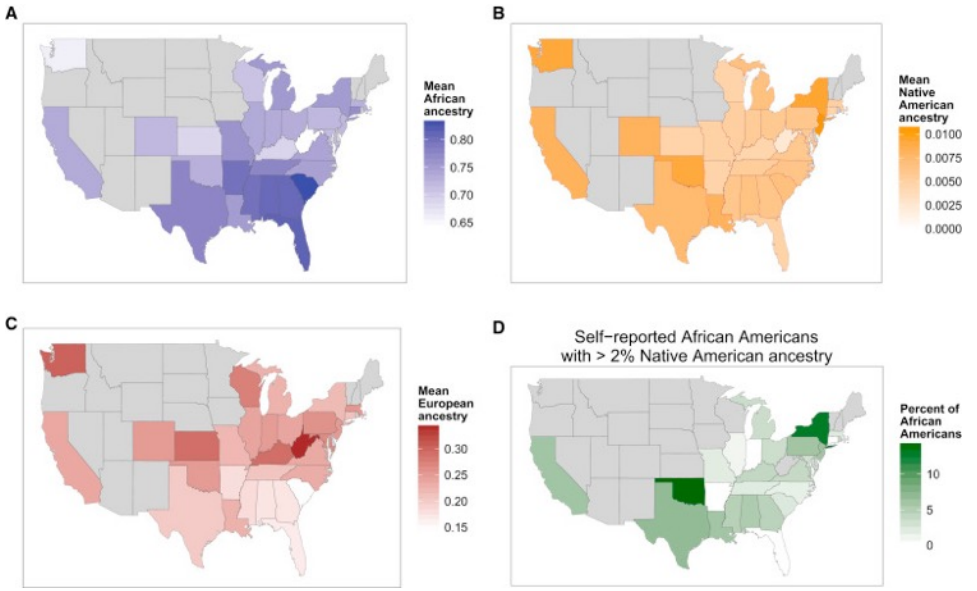


Figure 1. The Distribution of Ancestry of Self-Reported African Americans across the US

Discussion question

In Zoom breakout rooms of 2-3, discuss the following :

Would you be interested in doing a DTC genetic test? Why or why not?

After ~5 minutes discussion, we will come back together as a group and have the small discussion groups report out

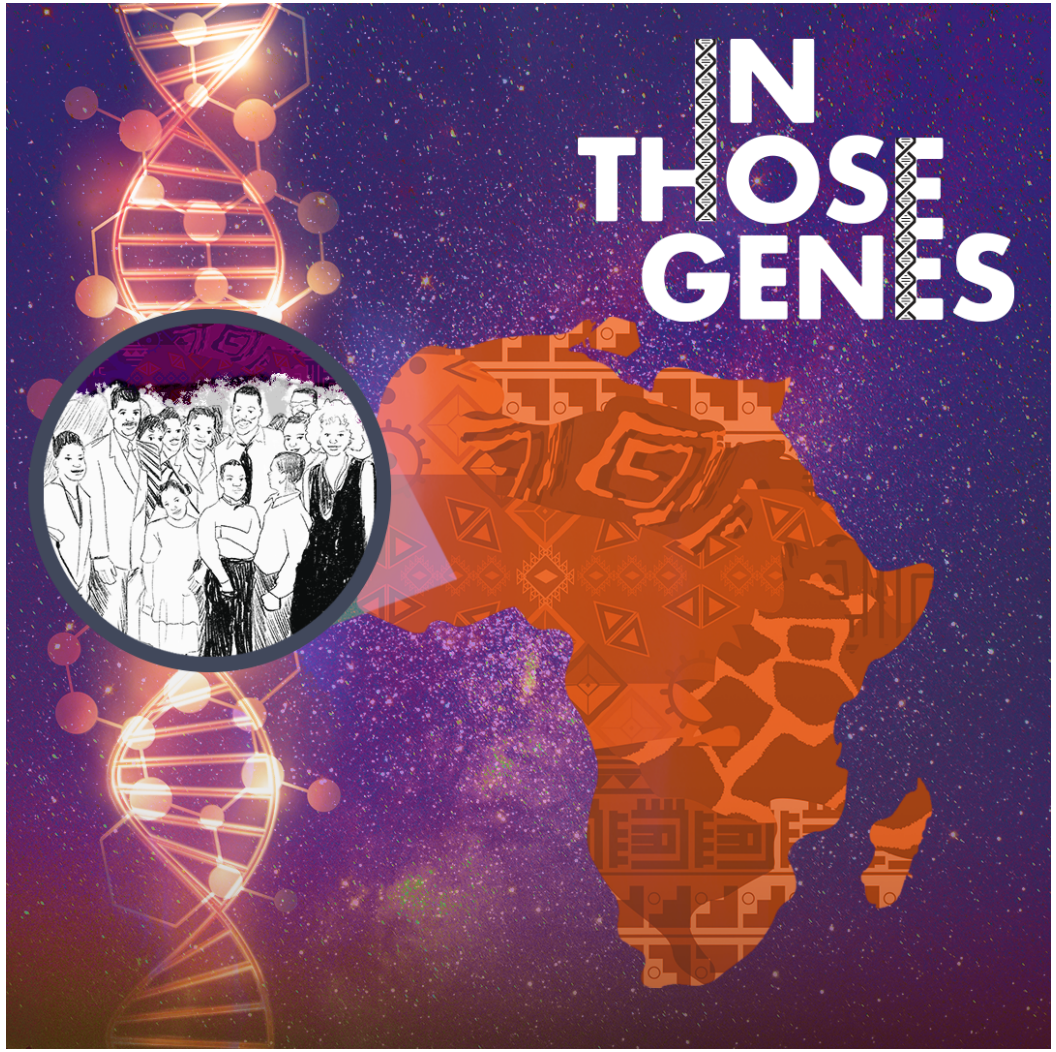
Podcast excerpt

"A hip-hop inspired podcast that uses genetics to uncover the lost identities of African descended Americans through the lens of Black culture."

Created by Dr. Janina Jeff

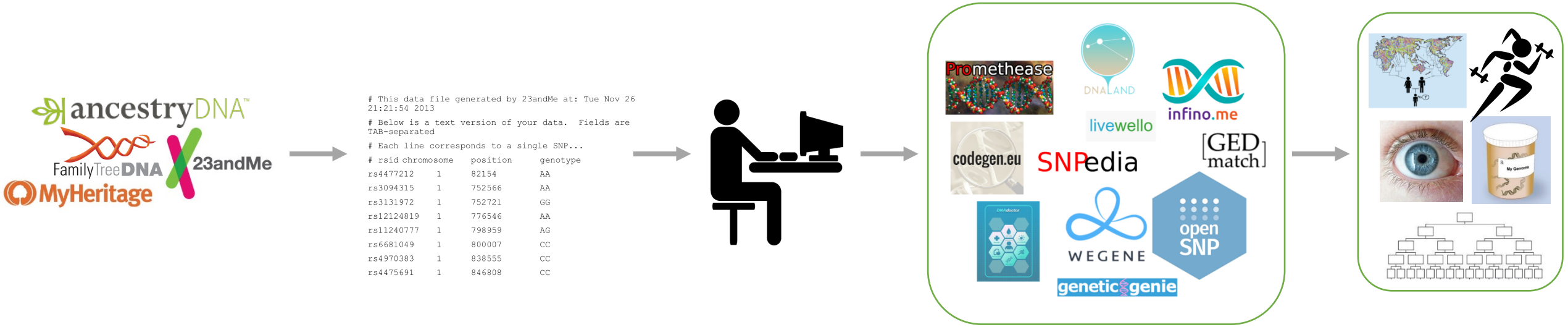
ASHG Advocacy Award 2020

Episode context – Janina interviewing Black elders in her home community of New Orleans on their perception of genetic testing



Third-party interpretation tools

- Online tools to analyze previously generated genetic data
- Do not require access to biospecimens or genotyping facilities
- Accept DTC “raw” genetic data files
- Similar to DTC companies, can return info across range of categories:
  - Genetic ancestry, genealogy, traits, health, diet & fitness



Raw/uninterpreted genetic data

```
# This data file generated by 23andMe at: Tue Nov 26 21:21:54 2013

# Below is a text version of your data.  Fields are TAB-separated

# Each line corresponds to a single SNP...

# rsid chromosome   position      genotype
rs4477212    1      82154         AA
rs3094315    1      752566        AA
rs3131972    1      752721        GG
rs12124819   1      776546        AA
rs11240777   1      798959        AG
rs6681049    1      800007        CC
rs4970383    1      838555        CC
rs4475691    1      846808        CC
```

each row is a genetic variant

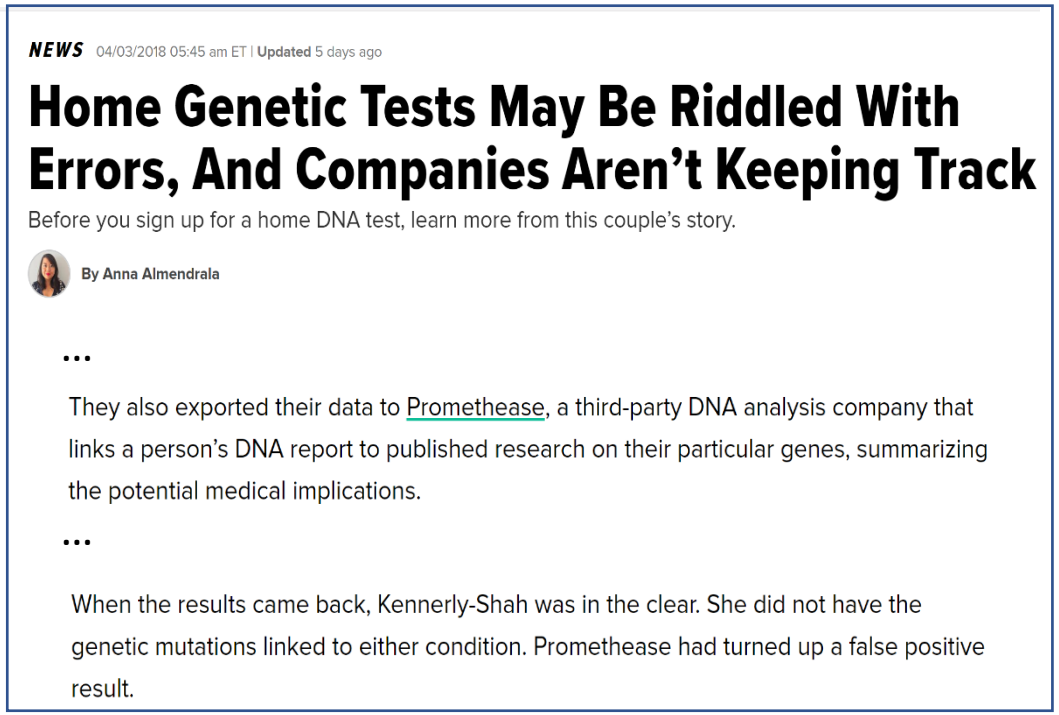
genotype at these variants

...plus ~one million more rows...

What's at stake?

- Third-party interpretation (TPI) tools appear to be unregulated
- Is this a concern? Helpful to have:
  - Deeper knowledge of what tools exist and how they work
  - Empirical evidence of potential harms and benefits to users of these tools
  - Understanding of how technical and scientific components should inform potential responses from policymakers

TPI may lead to false positive health results



NEWS 04/03/2018 05:45 am ET | Updated 5 days ago

Home Genetic Tests May Be Riddled With Errors, And Companies Aren't Keeping Track

Before you sign up for a home DNA test, learn more from this couple's story.

By Anna Almendrala

...

They also exported their data to Promethease, a third-party DNA analysis company that links a person's DNA report to published research on their particular genes, summarizing the potential medical implications.

...

When the results came back, Kennerly-Shah was in the clear. She did not have the genetic mutations linked to either condition. Promethease had turned up a false positive result.

The New York Times

Opinion

23andMe Said He Would Lose His Mind. Ancestry Said the Opposite. Which Was Right?

By Laura Hercher

Ms. Hercher is a genetic counselor.

Sept. 15, 2018

The New York Times

The Online Gene Test Finds a Dangerous Mutation. It May Well Be Wrong.

Third-party analysis of raw DNA is not as rigorous as that done in a certified laboratory. But many consumers don't understand that their results are not conclusive.

By Gina Kolata

July 2, 2018

TPI tools may be used by law enforcement

genomeweb

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Home » Tools & Technology » Microarrays & Multiplexing » Forensic Genomics Market Advances Due to Consumer Databases, Technology

Forensic Genomics Market Advances Due to Consumer Databases, Technology Innovation

Jan 09, 2020 | Justin Petrone

Premium *Save for later*

NEW YORK – As 2020 dawns, the forensic genomics market is poised for growth as companies aim to harness the power of consumer databases coupled with advances in sequencing.

For some industry observers, the health market has often been seen as the next logical step for companies that offer consumer genomics services. 23andMe served the market from the launch of its Personal Genome Service in 2007, and Ancestry and MyHeritage last year began offering their users health information in addition to ancestry results.

SCIENCE

How a Genealogy Website Led to the Alleged Golden State Killer

Powerful tools are now available to anyone who wants to look for a DNA match, which has troubling privacy implications.

SARAH ZHANG APRIL 27, 2018

MORE STORIES

Solving a Murder Mystery With Ancestry Websites
CIARA O'ROURKE

The False Promise of DNA Testing
MATTHEW SHAER

23andMe Wants Its DNA Data to Be Less White
SARAH ZHANG

future tense

We're Entering a New Phase in Law Enforcement's Use of Consumer Genetic Data

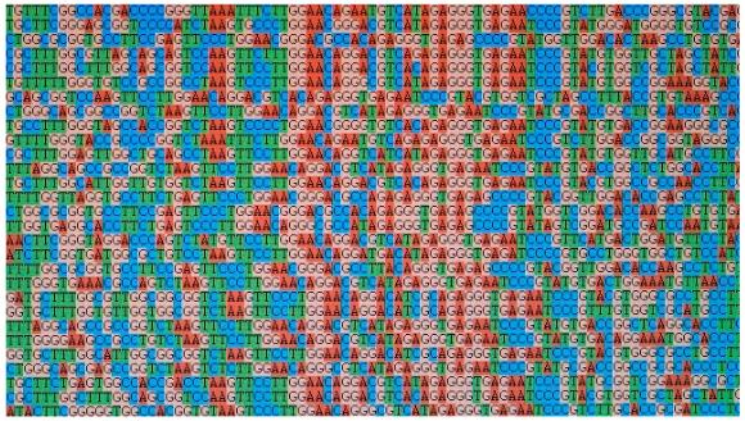
The favorite database for solving cold cases is now owned by a for-profit company. This could change everything.

By NILA BALA DEC 19, 2019 • 7:30 AM

FEBRUARY 4, 2020

About half of Americans are OK with DNA testing companies sharing user data with law enforcement

BY ANDREW PERRIN



(alanphillips via Getty Images)

The New York Times

Your DNA Profile is Private? A Florida Judge Just Said Otherwise

Privacy experts say a warrant granted in Florida could set a precedent, opening up all consumer DNA sites to law enforcement agencies across the country.

What is investigative genetic genealogy (IGG)?

"…the science of using genetic and genealogical methods to generate leads for law enforcement entities investigating crimes and identifying human remains"

- International Society of Genetic Genealogy Wiki, https://isogg.org/wiki/Investigative_genetic_genealogy_FAQ

Also referred to as *forensic genetic genealogy (FGG)*

Key features of IGG/FGG

When traditional methods have not produced a suspect

- Use of non-governmental databases containing
- …high density genetic data that enables
  - e.g., data from genotyping array with 500K-1M SNPs
- …long range familial searching paired with
- …traditional genealogical methods that
- …generates investigative leads requiring CODIS confirmation

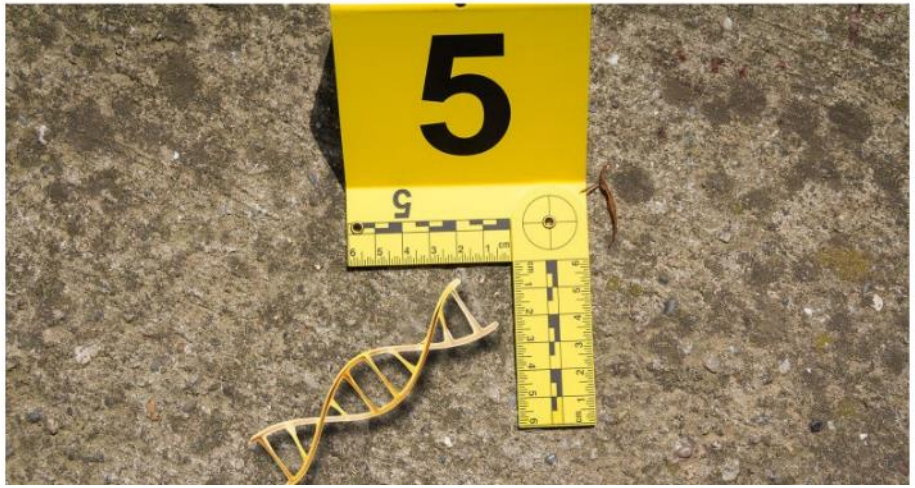


Image: *Slate* magazine

Databases that enable IGG

DTC companies

- Family Tree DNA
  - Only DTC company explicitly cooperating with law enforcement (LE) requests
  - Customers automatically opted in, unless EU resident
- My Heritage requires court order for LE usage
- 23andMe and AncestryDNA report to actively resist LE requests, including subpoenas
  - Both 23andMe and Ancestry DNA maintain transparency reports disclosing LE requests

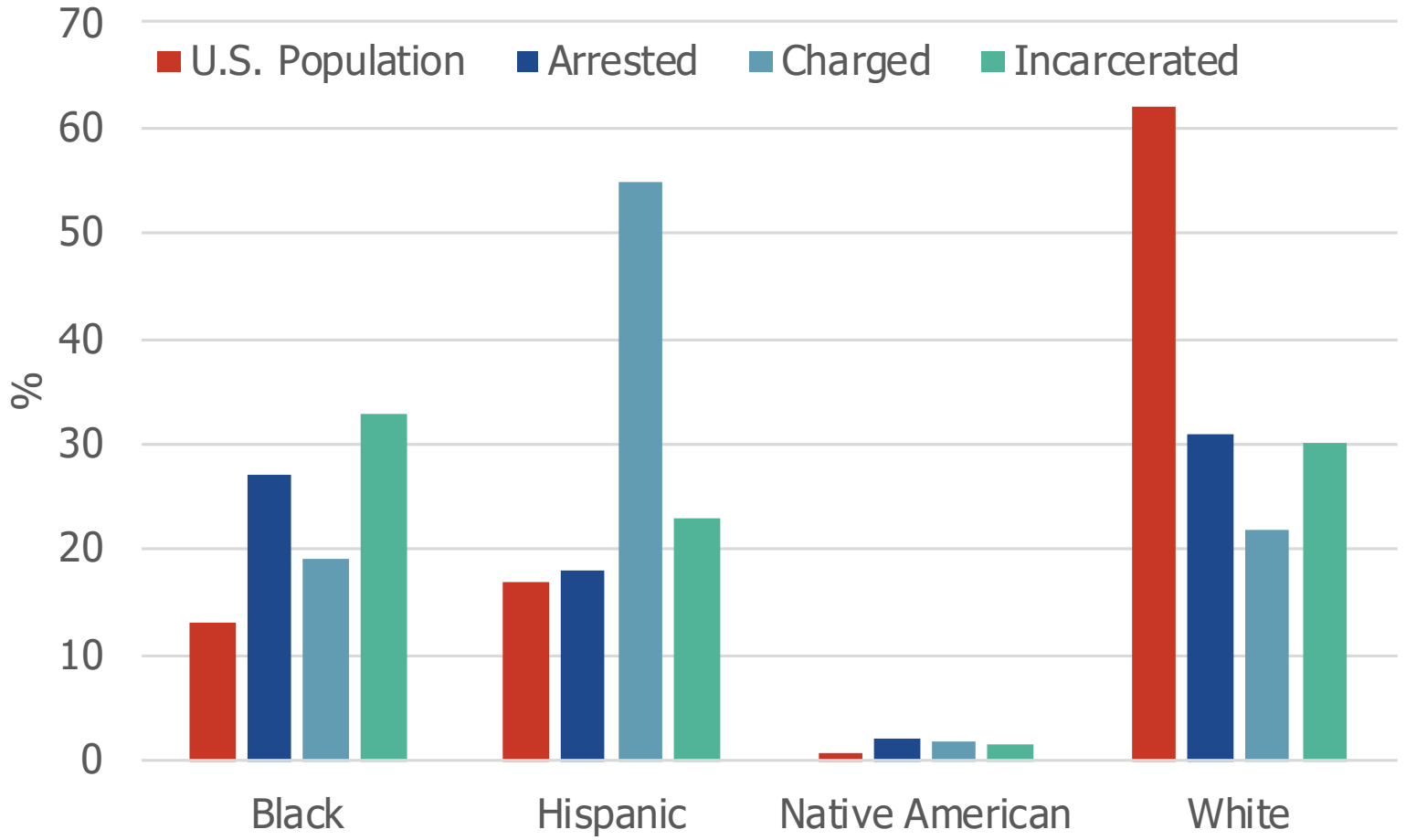
Third-party tools

- Users upload "raw" data files from DTC companies
- GEDmatch - publicly available genealogy site
- Apparently responsible for most of IGG

https://learn.familytreedna.com/ftdna/law-enforcement-faq/; Greytak, Moore, Armentrout 2019

Slide courtesy of Personal Genetics Education Project, https://pged.org/lesson-plans/#crime

Communities of color disproportionately represented in governmental DNA databases



Data from https://www.bjs.gov/content/pub/pdf/p16.pdf, https://www.bjs.gov/content/pub/pdf/fjs1314.pdf, and https://ucr.fbi.gov/crime-in-the-u.s/2016/crime-in-the-u.s.-2016/topic-pages/tables/table-21 (accessed June 12, 2019)

GEDmatch in flux

- April 2018 – GEDmatch reported as tool used to crack GSK case
- May 2018 – explicitly allow data upload by LE
  - for violent crimes only: homicide and sexual assault
- May 2019 – changed TOS to require opt-in for use by LE
  - Also expanded definition of violent crime
  - Reduced available search space from >1M to <200K
- Nov 2019 – Florida judge issues search warrant for GEDmatch
  - So does opt-in/opt-out even matter?
- Dec 2019 – GEDmatch bought by forensic genomics company Verogen

Ram 2019, *Slate;* Hill and Murphy 2019, *New York Times;* Bala 2019, *Slate*

THANK YOU!

DISCUSSION, Q&A

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